



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
WASHINGTON, D. C. 20231

6/10/79  
4-8-80  
335  
330 800

In re application of:

Robert E. Fischell ✓

For: Implantable, Programmable  
Medication Infusion System

335

Serial No.: 034155 ✓

Filed: April 27, 1979 ✓

LETTER

Hon. Commissioner of Patents and Trademarks  
Washington, D.C.

11  
8

Sir:

Pursuant to Applicant's continuing duty under Rule 56, Applicant has previously submitted two letters (including lists of patents and publications) which relate to the above-identified invention. A lengthy list of articles (provided with the second letter of July 16, 1979) was cited in a limited distribution report as including articles "relevant to drug infusion systems." To facilitate the Examiner's review of these references, Applicant offers the following discussion of the apparently more significant articles. Copies of articles not previously provided are enclosed herein.

Irsigler et al and Pickup et al each disclose a portable dosage-regulating apparatus having an electronic control box. No implantation is suggested. Specific circuitry or means for effecting safe operation are not set forth.

Fogt et al teaches a closed-loop infusion system for detecting glucose level, determining by computer means the amount of medication required based on that level, and delivering medication. The "heart of the system" is the

glucose level analyzer which is not a claimed part of the present invention. The safety features, structure, patient-physician programming and communication, and open loop design of the present invention are clearly absent from this reference.

Thomas et al discloses an implantable insulin delivery pump. The advantages of a piezoelectric pump providing a train of pulses at "resonance" are discussed. Programming infusion, providing redundant safeguards, telemetry communication, and various claimed pump features are not detailed in the reference.

Blackshear (in Scientific American and other cited articles) discusses the Infusaid implantable pump (by Metal Bellows Company of Sharon, Massachusetts) which continuously provides drug to a patient. No mention of dosage limiting, programmability, leakage prevention, or electronics for control or safety purposes is made in the reference.

Kraegan et al teaches an artificial pancreas which employs computer means in conjunction with a peristaltic pump to infuse drugs. Also a "module" independent of the computer means is included therein to monitor the pulse repetition rate of the pump. What the module is and how it functions is not discussed. The peristaltic pump does not provide the safety and power advantages of the pump claimed in the present invention. Clemens et al also employs a peristaltic pump.

Marliss et al discloses an artificial pancreas wherein infusion rates were determined by glucose measurements. Continuous, not commanded, infusion is disclosed in response to various algorithms based on glucose levels.

Santiago (Diabetes, Volume 28, No. 1) is provided for its discussion of insulin delivery systems and its review of the

Metal Bellows and Thomas et al pump devices. Santiago states that (as of 1979) existing infusion pumps "do not provide a mechanism for varying the rates of infusion delivery." The programmable feature of the present invention addresses this deficiency.

The above-discussed references are believed to be the more relevant references cited. A copy of each publication discussed above or in the patent application (and not previously provided) is enclosed herein. Other references included in the previously submitted list are material as providing background, alternative approaches (such as closed-loop artificial pancreas cells), clinical experimentation and comments suggesting the possible applications for and significance of the present invention, and general medical considerations. Such references are not discussed and are not provided.

Applicant also wishes to again make clear that the references cited are not necessarily prior art. Some of the cited articles post-date the invention as well as the filing of the patent application relating to the present invention.

Respectfully submitted,



Robert E. Archibald  
Attorney of Record  
Registry No. 20,934

Phone:

953-7100, X7604

CLLP-E80-72  
March 5, 1980

## REFERENCES

- ✓ A. Michael Albisser, et al, "Studies with an Artificial Endocrine Pancreas", Arch Intern Med, Vol. 137, May 1977
- ✓ Walter E. Stamm, "Infections Related to Medical Devices", Annals of Internal Medicine, 89, 1978
- ✓ Thomas D. Rohde, et al, "One Year of Heparin Anticoagulation", Minn. Med., October 1977
- ✓ T. D. Rohde et al, "Protracted Parenteral Drug Infusion in Ambulatory Subjects Using an Implantable Infusion Pump", Trans. Am. Soc. Artif. Intern. Organs, Vol. 22, October 1977
- ✓ W. D. Kaplan et al, "Intra-Arterial Radionuclide Infusion: A New Technique to Assess Chemotherapy Perfusion Patterns", Cancer Treatment Reports, Vol. 62, May 1978
- ✓ W. J. Spencer, "For Diabetics: An Electronic Pancreas", IEEE Spectrum, Vol. 15, June 1978
- ✓ Karl Irsigler et al, "Long-Term Continuous Intravenous Insulin Therapy with a Portable Insulin Dosage-regulating Apparatus", Diabetes, Vol. 28, March 1979
- ✓ J. C. Pickup et al, "Continuous Subcutaneous Insulin Infusion: An Approach to Achieving Normoglycaemia", British Medical Journal, Vol. 1, 1978
- Eric J. Fogt, et al, "Development and Evaluation of a Glucose Analyzer for a Glucose-Controlled Insulin Infusion System", Clin. Chem, 1978, Vol. 24
- L. J. Thomas, et al, "Prototype for an Implantable Micropump Powered by Piezoelectric Disk Benders", Trans. Amer. Soc. Artif. Int. Organs, Vol. 21, 1975
- Perry J. Blackshear, "Implantable Drug-Delivery Systems", Scientific American, 1979
- Perry J. Blackshear, et al, "The Effect of Continuous Heparin Infusion for one Year on Serum Cholesterol and Triglyceride Concentrations in the Dog", Atherosclerosis, Vol. 26, 1977
- Perry J. Blackshear et al, "One Year of Continuous Heparinization in the Dog Using a Totally Implantable Infusion Pump", Surgery, Gynecology & Obstetrics, Vol. 141, August 1975
- E. W. Kraegen, et al, "Control of Blood Glucose in Diabetics Using an Artificial Pancreas", Aust. N.Z.J. Med., Vol. 7, 1977
- Errol B. Marliss, et al, "Normalization of Glucemia in Diabetics During Meals with Insulin and Glucagon Delivery by the Artificial Pancreas", Diabetes, Vol. 26, July 1977
- Julio V. Santiago, et al, "Closed-loop and Open-loop Devices for Blood Glucose Control in Normal and Diabetic Subjects", Diabetes, Vol. 28, 1979
- A. H. Clemens, et al, "The Development of Biostator, a Glucose Controlled Insulin Infusion System", Horm. Metab. Res. Suppl., Vol. 7, 1977